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EXAMINER	
SWOPE, SHERIDAN	

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1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/571,515	FOSTER ET AL.	
	Examiner	Art Unit	
	SHERIDAN SWOPE	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 December 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58-97* is/are pending in the application.

4a) Of the above claim(s) *59 and 76-97* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *58 and 60-75* is/are rejected.

7)☒ Claim(s) *58 and 62* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 December 2008* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' amendment of December 15, 2008, in response to the Action of August 15, 2008, is acknowledged. It is acknowledged that Claims 58 and 60-75 have been amended. Claims 58-97 are pending. Claims 59 and 76-97 were previously withdrawn from further consideration pursuant to 37 CFR 1.142(b). Claims 58 and 60-75 are hereby reexamined.

Drawings-Objections

Objection to Figures 5-7, because the lanes are not labeled or clearly described, is maintained. It is acknowledged the lanes of Figures 5-7 have been numbered; however, neither the drawings nor the legends thereto clearly describe said lanes.

Claims-Objections

Claim 58, line 6, and Claim 62, line 3, are objected to for "target cell, said binding site", which should be corrected to "target cell, wherein said binding site".

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Double Patenting

Provisional rejection of Claims 58, 60-63, 74, and 75 under the judicially created doctrine of obviousness-type double patenting, is maintained.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Rejection of Claims 58 and 60-75 under 35 U.S.C. 112, first paragraph/enablement, for the reasons explained in the prior action, is maintained. In support of their request that said rejection be withdrawn, Applicants provide the following arguments.

(A) The specification exemplifies the preparation of conjugates having a range of targeting moiety, protease, and translocation domains, well beyond that of IL-13 targeting agonist and the catalytic and targeting moiety domains described in Example 8. Specifically, Example 3 discloses the preparation of an IL-13 - LH_N/C conjugate, Example 11 discloses the preparation of an Insulin - LH_N/B conjugate, Example 15 discloses the preparation of a MCD peptide - LH_N/C conjugate, Example 19 discloses the preparation of an IL-4 - LH_N/C conjugate, Example 22 discloses the preparation of a TNFα - LH_N/C conjugate, and Example 25 discloses the preparation of an EGF - LH_N/C conjugate. The structures of these fragments have been extensively characterized in the art (see, e.g., page 1, line 37 to page 3, line 37 of the present specification, and page 12, line 13 to page 15, line 22). Thus, the structures of these fragments and the expected tolerance of specific amino acids to modification would be well-known to the skilled person in the art. Specific disclosure thereof is not required to be enabling to the skilled person. Therefore, applicants respectfully submit that these examples provide enabling disclosure supporting the claimed invention.

(B) A skilled person, without undue experimentation, would be able to identify alternative targeting moieties, translocation domains, and proteases to generate a conjugate according to the invention for the following reasons.

(C) Methods for making fusion proteins are well-known in the art and the specification describes how to use the clostridial neurotoxin domains to make a variety of fusion proteins.

These arguments are not found to be persuasive for the following reasons.

(A) Reply: It is acknowledged that Examples 3, 11, 15, 19, 22, and 25 disclose fusion proteins having said designations. However, said examples do not disclose that the fusion protein have the desired activities of translocating the fusion protein from the endosome to the cytosol, cleaving a protein of the exocytic fusion apparatus, and being non-cytotoxic. In addition, the specification fails to define the terms LH_N/C and LH_N/B and said terms are not known in the art (see Entrez enclosures). Therefore, the skilled artisan would not be enabled to make and use any targeting fusion protein comprising LH_N/C or LH_N/B domains. Moreover, even if the specification was enabling for any targeting fusion protein comprising LH_N/C or LH_N/B domains, which it is not, the claims are not limited to fusion proteins comprising said domains. As explained in the prior action, Claims 58 and 60-74 are so broad as to encompass any method for making any conjugate comprising any targeting agonist, any non-toxic protease, and any translocation domain, wherein the conjugate inhibits exocytic fusion of any vesicle in any cell, while Claim 75 is so broad as to encompass any method for making any conjugate comprising any targeting agonist, any non-toxic clostridial neurotoxin protease, and any translocation domain, wherein the conjugate inhibits exocytic fusion of any vesicle in any cell. For the reasons explained in the prior action, the scope of these claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of methods for making an extremely large number of conjugates, as broadly encompassed by the claims.

(B) Reply: It is acknowledged that the skilled person would be able to identify alternative targeting moieties. Nonetheless it is noted that Applicants' rebuttal of the rejections under 35 USC 103(a), which seems to argue that selecting an appropriate targeting moiety is not well-known in the art, states the following (pg27).

> "An inventive step underlying the present invention rests in the selection of a particular type of targeting moiety (TM) that is used to target the conjugate to the target cell. Specifically, the targeting moiety is an agonist that increases exocytic fusion in the target cell. Applicants have unexpectedly found that taking this entirely counterintuitive step (i.e., targeting the conjugate using a targeting moiety that stimulates the very process that the conjugate is intended to inhibit) has a number of surprising advantages."

Domains capable of translocating a protein across the endosomal membrane and into the cytosol were not well-known at the time of filing. As evidence thereof, a search of PubMed for the string "'translocation domain' endosome review" identified no articles, while the string "'translocation domain' endosome" identified only eight articles published prior to the priority date of the instant invention (see enclosures). Said eight articles disclosed only two domains capable of translocating a protein across the endosomal membrane and into the cytosol: Pseudomonas exotoxin A and diphtheria toxin endosomal translocation domains. The instant claims encompass making a fusion protein comprising any endosomal translocation domain, having any structure. While some methods for screening for endosomal translocation in some cell types were known, it is not routine in the art to screen an essentially unlimited number of polypeptides for the desired activity of endosomal translocation, as encompassed by these claims.

The art teaches that at least 15 proteins are involved in exocytic fusion in humans, while at least seven proteins are involved in yeast (Teng et al, 2001). The instant invention encompasses making a fusion protein comprising any protease, having any structure, wherein the

protease cleaves any protein involved in exocytic fusion and is non-cytotoxic. It is acknowledged that recombinant and mutagenesis techniques as well as protein purification methods were known. It is also acknowledged that methods for detecting protein cleavage were known. However, it is not routine in the art to screen an essentially unlimited number of proteins having any structure for the desired activity of cleaving any one of the large number of proteins involved in exocytic fusion in any organism and then further test the identified protease for lack of cytotoxicity. Moreover, methods for testing any protein for cleavage of any protein involved in exocytic fusion is labor intensive. The specification does not enable any person skilled in the art to make and use the full scope of any fusion protein comprising any protease, having any structure, wherein the protease cleaves any protein involved in exocytic fusion in any cell and is non-cytotoxic, as encompassed by these claims.

(C) Reply: It is acknowledged that methods for making fusion proteins were well-known in the art. The instant claims are not limited to use of clostridial neurotoxin domains to make fusion proteins.

For these reasons and those explained in the prior action, rejection of Claims 58 and 60-75 under 35 U.S.C. 112, first paragraph/enablement, is maintained.

Written Description

Rejection of Claims 58 and 60-75 under 35 U.S.C. 112, first paragraph/written description, for the reasons explained in the prior action, is maintained. In support of their request that said rejection be withdrawn, Applicants provide the following arguments.

(D) As detailed above (Enablement), the specification discloses conjugates with a range of targeting moiety, protease, and translocation domains (see Examples 3, 11, 15, 19, 22, and 25).

(E) Also as described above, it would be a routine matter for a skilled artisan to identify alternative targeting moieties, translocation domains, and proteases to generate conjugates according to the invention. Thus, the specification provides sufficient description such that a skilled artisan would recognize that applicants were in possession of the claimed invention.

These arguments are not found to be persuasive for the following reasons.

(D) Reply: It is acknowledged that Examples 3, 11, 15, 19, 22, and 25 disclose fusion proteins having the designations IL-13 - LH_N/C, Insulin - LH_N/B conjugate, MCD peptide - LH_N/C, IL-4 - LH_N/C, TNFα - LH_N/C, and EGF - LH_N/C. However as explained above, said examples do not disclose that the fusion proteins have the desired activities of translocating the fusion protein from the endosome to the cytosol, cleaving a protein of the exocytic fusion apparatus, and being non-cytotoxic. As explained in the prior action, Claims 58 and 60-74 are so broad as to encompass a genus of any method for making any conjugate comprising any targeting agonist, any non-toxic protease, and any translocation domain, wherein the conjugate inhibits exocytic fusion of any vesicle in any cell, while Claim 75 is so broad as to encompass a genus of method for making any conjugate comprising any targeting agonist, any non-toxic clostridial neurotoxin protease, and any translocation domain, wherein the conjugate inhibits exocytic fusion of any vesicle in any cell. For the reasons explained in the prior action, the specification fails to describe said genera in a manner such that the skilled artisan could recognize they were in possession of the full scope of the invention.

(E) Reply: The reasons neither the prior art nor the specification enable the skilled artisan to make and use the full scope of the recited invention is explained above and in the prior action. Thus, the specification fails to provide sufficient description such that a skilled artisan would recognize that Applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Rejection of Claims 58, 62, 64, 74, and 75 under 35 U.S.C. 102(a,e) as being anticipated by Bigalke et al, 2004, for the reasons explained in the prior action, is maintained. In support of their request that said rejection be withdrawn, Applicants provide the following arguments.

(F) The pivotal step underlying the claimed method is the selection of an agonist that is used to target the conjugate to the target cell, wherein the agonist increases exocytic fusion in the target cell. The Bigalke reference fails to teach at least the element of identifying an agonist that increases exocytic fusion in the target cell, as recited in Claim 58.

(G) The aim of the Bigalke reference is to inhibit exocytic fusion in the target cells.

(H) The IgE used as a targeting moiety in Bigalke does not induce exocytic fusion in the target cell. The presence of a separate allergen is required before exocytic fusion will occur.

Likewise, the targeting moiety that includes an inactive Mast Cell Degranulating peptide taught by Bigalke, is not acting as an agonist that increases exocytic function in the target cell.

These arguments are not found to be persuasive for the following reasons.

(F) Reply: It is acknowledged that the claims include a step of identifying an agonist targeting moiety that increases exocytic fusion in the target cell. However, Claims 58, 62, 64, 74, and 75 fail to recite any methodological limitations for said "identifying". Thus, "identifying" encompasses searching the prior art databases for appropriate agonist targeting moieties, as performed by Applicants (for instance, in Example 1).

(G) Reply: It is acknowledged that, as for Applicants, the ultimate aim of Bigalke et al is to inhibit exocytic fusion in target cells. Also, as for Applicants, Bigalke et al teach, as explained in the prior action, using a conjugate comprising a targeting moiety linked to a protease and a translocation domain, wherein the conjugate is taken up by the cell via receptor-mediated endocytosis, translocated from the endosome to the cytosol, and cleaves a protein of the fusion apparatus, thus accomplishing said ultimate aim.

(H) Reply: It is acknowledged that IgE does not induce exocytosis in the absence of an allergen. Nonetheless, as taught by Bigalke et al, the skilled artisan would know to use the IgE-containing fusion protein in the presence of an allergen to provide agonist properties to their IgE domain.

It is acknowledged that the Mast Cell Degranulating peptide of by Bigalke et al is inactive.

For these reasons and those explained in the prior action, rejection of Claims 58, 62, 64, 74, and 75 under 35 U.S.C. 102(a,e) as being anticipated by Bigalke et al, 2004, is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Rejection of Claims 58, 60-65, 67-69, and 72-75 under 35 U.S.C. 103(a) as being unpatentable over Bigalke et al, 2004 in view of Skeberdis et al, 2001, for the reasons explained in the prior action, is maintained. Rejection of Claims 58, 60-65, 67, 70, 71, 74, and 75 under 35 U.S.C. 103(a) as being unpatentable over Bigalke et al, 2004 in view of Foran et al, 1999 for the reasons explained in the prior action, is maintained. Rejection of Claim 66 under 35 U.S.C. 103(a) as being unpatentable over Bigalke et al, 2004 in view of Yoshimaru et al, 2002, for the reasons explained in the prior action, is maintained.

In support of their request that said rejections be withdrawn, Applicants provide the following arguments.

(I) The claimed method includes a step of identifying a targeting moiety agonist that increases exocytic fusion in the target cell. The pivotal step underlying the claimed method is the selection of a particular type of targeting moiety that is used to target the conjugate to the target cell. The targeting moiety binds the fusion protein to a site on the target cell, thereby mediating endocytosis into the endosome.

(J) Bigalke teaches away from using an agonist as part of a toxin conjugate for inhibition or reduction of exocytic fusion in a target cell, as recited in Claim 58. This technical feature is therefore very different from the methods described in the Bigalke reference, which relate to

conventional re-targeting technology, and which do not teach or suggest any additional requirement for the targeting moiety to be an agonist of the target cell.

(K) Applicants have unexpectedly found that taking this entirely counterintuitive step (i.e., targeting the conjugate using a targeting moiety that stimulates the very process that the conjugate is intended to inhibit) has a number of surprising advantages. By way of example, the present Inventors have identified that the use of an agonist targeting moiety can confer preferential binding and/or internalization properties on a conjugate of the present invention, which may result in more efficient delivery of the protease component to the target cell. In addition, the use of an agonist as a targeting moiety can be self-limiting with respect to side-effects (see page 8). Applicants respectfully submit that neither the references nor the general knowledge within the art provide any guidance to make this counterintuitive step of utilizing an agonist to prepare conjugate for inhibition or reduction of exocytic fusion in a cell.

(L) The deficiencies noted in Bigalke, not using an agonist as part of a conjugate, are not cured by the teachings of the Skeberdis, Foran, or Yoshimaru references.

(M) There is no suggestion in Skeberdis or Foran that insulin should be used, or is even capable of being used, as part of a conjugate to inhibit the exocytic process.

(N) The Yoshimaru reference simply describes the use of ELISA to detect the release of histamine from mast cells after stimulation using IgE and specific antigen. This reference provides no teaching whatsoever towards using an agonist as a targeting moiety to inhibit or reduce exocytic fusion in target cells.

These arguments are not found to be persuasive for the following reasons.

(I) Reply: It is acknowledged that the claims include a step of identifying an agonist targeting moiety that increases exocytic fusion in the target cell. However, Claims 58, 62, 64, 74, and 75 fail to recite any methodological limitations for said "identifying". Thus, "identifying" encompasses searching the prior art databases for appropriate agonist targeting moieties, as performed by Applicants (for instance, in Example 1).

It is acknowledged that Claims 60-73 recite specific steps to be performed for identifying an agonist targeting moiety. However, as explained in the prior action, Foran et al (Fig 6) teach identifying insulin as an agonist that increases plasma membrane expression of the GLUT4 transporter via exocytosis by (a) identifying a putative agonist molecule; (b) contacting the target cell with said putative agonist molecule; and (c) confirming said putative agonist molecule is an agonist by identifying an increase in exocytic fusion in the target cell, as recited in Claims 60-73.

(J) Reply: Applicants' assertion that Bigalke et al teaches away from using an agonist as part of a toxin conjugate for inhibition or reduction of exocytic fusion in a target cell is not convincing since, Bigalke et al teaches use of a co-agonist (IgE; col 3, lines 3-12) for preparing an agent comprising IgE linked to the translocation and catalytic domains of a clostridial neurotoxin, which is known to cleave proteins of the secretion process (col 3, lines 24-42).

(K) Reply: Applicants' assertion, that taking the step of targeting the conjugate using a targeting moiety that stimulates exocytosis is entirely counterintuitive, is not found to be convincing. The skilled artisan would know that essentially all receptor-mediated endocytosis is via an agonist binding to its receptor. Thus, to get a conjugate into a secretory cell, the skilled artisan would be motivated to use a conjugate comprising an agonist. In secretory cells, said

binding would, more likely than not, induce exocytosis. The skilled artisan would also know that said mechanism of conjugate uptake, receptor mediated endocytosis followed by secretion, would in no way affect the ability of the internalized conjugate to subsequently cleave a protein of the exocytic fusion process.

It is acknowledged that, as was known in the art, the use of an agonist targeting moiety confers preferential binding and/or internalization properties on a conjugate and can be self-limiting with respect to side-effects due to receptor down-regulation (Knutson, 1991). For these reasons and those explained in the prior action, the instant invention would not have been counterintuitive to the skilled artisan.

(L) Reply: The reason Bigalke et al does teach using an agonist as part of a conjugate, as explained in the prior action and in (H) and (J), above. Each of Skeberdis et al and Foran et al also teach using an agonist as part of a conjugate.

(M) Reply: The instant rejection does not require that Skeberdis et al or Foran et al suggest that insulin should be used as part of a conjugate to inhibit the exocytic process. The instant rejection requires the teachings of Skeberdis et al and Foran et al; that insulin is an agonist that induces exocytosis of NMDA receptors and GLUT4, respectively. The skilled artisan would have been aware of the problems to be solved: treating deficiencies in learning and memory and deficiencies in glucose uptake. The skilled artisan would have been motivated to combine the teachings of Skeberdis et al or Foran et al with Bigalke et al to develop a conjugate comprising insulin and clostridial neurotoxin, which would be useful for modulating synaptic NMDA receptors or GLUT4, respectively.

(N) Reply: For rejection of Claim 66 under 35 USC 103(a), it is not required for Yoshimaru et al to teach using an agonist as a targeting moiety to inhibit or reduce exocytic fusion in target cells. If Yoshimaru et al did so teach, Claim 66 would be anticipated by Yoshimaru et al and rejected under 102. As explained in the prior action, the teaching of Yoshimaru et al, using ELISA to detect the release of histamine from mast cells after stimulation using IgE and specific antigen, in combination with the teachings of Bigalke et al supports the rejection of Claim 66 under 35 USC 103(a).

Allowable Subject Matter

No claims are allowable.

Applicant's amendment necessitated any new grounds of rejection presented in this Office action. Any new references were cited solely to support rejection(s) based on amendment or rebut Applicants' arguments. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Regarding filing an Appeal, Applicants are referred to the Official Gazette Notice published July 12, 2005 describing the Pre-Appeal Brief Review Program.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages. It is also requested that the serial number of the application and date of amendment be referenced on every page of the response.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Nashed can be reached on 571-272-092834. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SHERIDAN SWOPE/
Primary Examiner, Art Unit 1652